Amendments t the Specification

After the title, please insert:

CROSS-REFERENCE TO RELATED APPLICATIONS

--This application is a divisional application of U.S. Patent Application Serial No. 09/272,835 filed March 19, 1999, from which priority is claimed under 35 U.S.C. 120, the entire contents of which are hereby incorporated by reference.--

Please amend the paragraph beginning at page 1, line 11 as follows:

Neurotrophic factors such as insulin-like growth factors, nerve growth factors, brain-derived neurotrophic factor, neurotrophin-3, -4/5 and -6, ciliary neurotrophic factor, GDNF, and neurturin have been proposed as potential means for enhancing specific neuronal cell survival, for example, as a treatment for neurodegenerative diseases such as amylotrophic lateral sclerosis, Alzheimer's disease, stroke, epilepsy, Huntington's disease, Parkinson's disease, and peripheral neuropathy. It would be desirable to provide additional therapy for this purpose. Protein neurotrophic factors, or neurotrophins, which influence growth and development of the vertebrate system, are believed to play an important role in promoting the differentiation, survival, and function of diverse groups of neurons in the brain and periphery. Neurotrophic factors are believed to have important signaling functions in neural tissues, based in part upon the precedent established with nerve growth factor (NGF). NGF supports the survival of sympathetic, sensory, and basal forebrain neurons both *in vitro* and *in vivo*. Administration of exogenous NGF rescues neurons from cell death during development. Conversely, removal or sequestration of endogenous NGF by administration of anti-NGF antibodies promotes such cell death (Heumann, *J. Exp. Biol.*, 132:133-150 (1987); Hefti, *J. Neurosci.* 6:2155-2162 (1986); Thoenen, *et al.*, ~~*Annu Rev. Physiol.*~~ Physiol. Rev., 60:~~284-335~~ 1284-1335 (1980)).

Please amend the paragraph beginning at page 1, line 25 as follows:

Additional neurotrophic factors related to NGF have since been identified. These include brain-derived neurotrophic factor (BDNF) (Leibrock, *et al.*, *Nature*, 341:149-152 (1989)); neurotrophin-3 (NT-3) (Kaisho, *et al.*, *FEBS Lett.*, 266:187

(1990); Maisonpierre, *et al., Science,* 247:1446 (1990); Rosenthal, *et al., Neuron,* 4:767 (1990), and neurotrophin 4/5 (NT-4/5) (~~Berkmeier~~ Berkemeier, *et al., Neuron,* 7:857-866 (1991)).

Please amend the paragraph beginning at page 17, line 33 and ending at page 18, line 10, as follows:

Glial cell line-derived neurotrophic facros ("GDNF") (Lin *et al., Science,* 260:1130-1132 (1993); WO 93/06116, which are incorporated herein in its entirety), is a potent survival factor for midbrain dopaminergic (Lin *et al.,* ~~Science, 260:1130-1132~~ (1993), *supra*; Strömberg *et al., Exp. Neurol.*, 124:401-412 (1993); Beck *et al., Nature*, 373:339-341 (1995): Kearns *et al., Brain Res.*, 672:104-111 (1995); Tomac *et al., Nature,* 373:335-339 (1995)), spinal motor (Henderson *et al., Science*, 266:1062-1064 (1994); Oppenheim *et al., Nature,* 373:344-346 (1995)); Yan *et al., Nature,* 373:341-344 (1995)), and noradrenergic neurons (Arenas *et al., Neuron*, 15:1465-1473 (1995)), which degenerate in Parkinson's disease (Hirsch *et al., Nature,* 334:345-348 (1988): Hornykiewicz, *Mt. Sinai J. Med.*, 55:11-20 (1988)), amyotrophic lateral sclerosis (Hirano, Amyotrophic Lateral Sclerosis and Other Motor Neuron Disease, P. Rowland, ed. (New York: Raven Press, Inc.) pp. 91-101 (1991), and Alzheimer's disease (~~Marcynuik~~ Marcyniuk *et al., J. Neurol. Sci.*, 76:335-345 (1986); Cash *et al., Neurology,* 37:42-46 (1987); Chan-Palay *et al., Comp. Neurol.*, 287:373-392 (1989)), respectively. Based on mice genetically engineered to lack GDNF, additional biological roles for GDNF have been reported: the development and/or survival of enteric, sympathetic, and sensory neurons and the renal system, but not for catecholaminergic neurons in the central nervous system (CNS) (Moore *et al., Nature* 382:76-79 (1996); Pichel *et al., Nature* 382:73-76 (1996); Sanchez *et al., Nature* 382:70-73 (1996)). Despite the physiological and clinical importance of GDNF, little is known about its mechanism of action.

Please amend the paragraph beginning at page 51, line 21 as follows:

Primers containing sense sequence GCCCGCGACCTCCACTGCTG (designated gfrp1; SEQ ID NO: 22) and ~~antiseesnse~~ antisense sequence CTGTGGGGAGCGGCGGCG (designated gfrp2.r.c; SEQ ID NO: 23) were used to

generate a 671 bp hybridization probe from the mouse GFRα3. Primers containing sense sequence CCTGAACCTATGGTAACTGG (SEQ ID NO: 24) and antisense sequence ACCCAGTCCTCCCTACC (SEQ ID NO: 25) were used to generate a 378 bp hybridization probe from the mouse GFRα3.--

Please amend the paragraph beginning at page 53 as follows:

In an alternative technique, mammalian *GFRα3* may be introduced into 293 cells transiently using the dextran sulfate method described by ~~Somparyac~~ Sompayrac *et al., Proc. Natl. Acad. Sci.*, ~~42~~ 78:7575 (1981). 293 cells are grown to maximal density in a spinner flask and 700 μg pRK5-*GFRα3* DNA is added. The cells are first concentrated from the spinner flask by centrifugation and washed with PBS. The DNA-dextran precipitate is incubated on the cell pellet for four hours. The cells are treated with 20 % glycerol for 90 second, washed with tissue culture medium, and re-introduced into the spinner flask containing tissue culture medium, 5 μg/ml bovine insulin and 0.1 μg/ml bovine transferrin. After about four days, the conditioned media is centrifuged and filtered to remove cells and debris. The sample containing expressed mammalian *GFRα3* can then be concentrated and purified by any selected method, such as dialysis and/or column chromatography.

Please amend the paragraph beginning at page 54, line 17 as follows:

Alternatively, expressed poly-his tagged GFRα3 can be purified by Ni^{2+}-chelate affinity chromatography as follows. Extracts are prepared from recombinant virus-infected Sf9 cells as described by ~~Rupert~~ Ruppert *et al., Nature* 362:175-179 (1993). Briefly, Sf9 cells are washed, resuspended in sonication buffer (25 mL Hepes, pH 7.9; 12.5 mM $MgCl_2$; 0.1 mM EDTA; 10% Glycerol; 0.1% NP-40; 0.4 M KCl), and sonicated twice for 20 seconds on ice. The sonicates are cleared by centrifugation, and the supernatant is diluted 50-fold in loading buffer (50mM phosphate, 300 mM NaC1, 10% Glycerol, pH 7.8) and filtered through a 0.45 Fm filter. A Ni^{2+}-NTA agararose column (commercially available from Qiagen) is prepared with a bed volume of 5 mL, washed with 25 mL of water and equilibrated with 25 mL of loading buffer. The filtered cell extract is loaded onto the column at 0.5 mL per minute. The column is washed to a baseline A_{280} with loading buffer, at

which point fraction collection is started. Next, the column is washed with a secondary wash buffer (50mM phosphate; 300 mM NaCl, 10% Glycerol, pH 6.0), which elutes nonspecifically bound protein. After reaching A_{280} baseline again, the column is developed with a 0 to 500 mM Imidazole gradient in the secondary wash buffer. One mL fractions are collected and analyzed by SDS-PAGE and silver staining or western blot with Ni^{2+}-NTA-conjugated to alkaline phosphatase (Qiagen). Fractions containing the eluted His_{10}-tagged GFRα3 are pooled and dialyzed against loading buffer.